Maintenance of neural progenitor cell stemness in 3D hydrogels requires matrix remodelling.

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Public Summary:
Neural progenitor cell (NPC) culture within three-dimensional (3D) hydrogels is an attractive strategy for expanding a therapeutically relevant number of stem cells. However, relatively little is known about how 3D material properties such as stiffness and degradability affect the maintenance of NPC stemness in the absence of differentiation factors. Over a physiologically relevant range of stiffness from approximately 0.5 to 50 kPa, stemness maintenance did not correlate with initial hydrogel stiffness. In contrast, hydrogel degradation was both correlated with, and necessary for, maintenance of NPC stemness. This requirement for degradation was independent of cytoskeletal tension generation and presentation of engineered adhesive ligands, instead relying on matrix remodelling to facilitate cadherin-mediated cell-cell contact and promote beta-catenin signalling. In two additional hydrogel systems, permitting NPC-mediated matrix remodelling proved to be a generalizable strategy for stemness maintenance in 3D. Our findings have identified matrix remodelling, in the absence of cytoskeletal tension generation, as a previously unknown strategy to maintain stemness in 3D.

Scientific Abstract:
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